

## REMARKS

Applicants claimed inventions provide efficient and effective methods for automatically generating and screening compounds. The methods improve efficiency by utilizing virtual compounds that are generated and evaluated *in silico* according to defined criteria. The criteria include thermodynamic properties, target accessibility, targeting to functional regions of target nucleic acid sequence, and uniform distribution to target nucleic acid sequence. Using Applicants' methods, active compounds are generated in an efficient manner and, at the same time, preferred sequences and regions of the target nucleic acid that are amenable to modulation are identified.

Claims 55, 56, 58-72, 74-87, and 99-102 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over a combination of five references. Specifically, the Office Action asserts that it would have been *prima facie* obvious for one skilled in the art to perform the desired compound design via the Agrafiotis and Uhlmann references, synthesize the compounds via the Dower reference, and then perform the assays as desired using the Haff and/or Harris references. Applicants maintain that the subject matter of the rejected claims is neither disclosed nor suggested by the collective teachings of the cited references.

Contrary to the Examiner's assertion, the Agrafiotis reference fails to disclose a method for generating or evaluating a virtual compound *in silico*. The Agrafiotis reference simply generates instructions for mixing chemical building blocks. Nowhere does Agrafiotis teach or suggest the concept of evaluating virtual compounds.

Although Applicants maintain that the Agrafiotis reference fails to disclose a method for generating or evaluating a virtual compound *in silico*, solely to advance prosecution, the pending claims have been amended to further distinguish Applicants' claimed inventions. Support for Applicants' amendment can be found in the specification at pages 19 through 22, and FIGS. 7, 8, and 9, for example.

Applicants' claims recite generating or evaluating *in silico* compounds according to thermodynamic property and at least one other criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof. Applicants provide a detailed description of each of these criteria in the specification (see pages 19-22, for example). The additional criteria recited in Applicants' claims for generating or evaluating *in silico*

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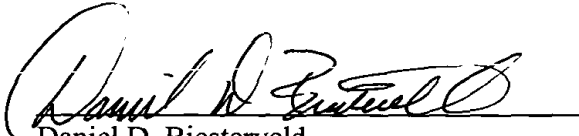
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compounds are not taught or suggested by any of the cited references, whether *in silico* or otherwise. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

### **Conclusion**

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 557-5963 if there are any questions regarding Applicants' claimed inventions.

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